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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,586	11/28/2000	Roman Sakowicz	UCSD-04871	9471

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	10

DATE MAILED: 10/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Applicati n No.	Applicant(s)	
	09/724,586	SAKOWICZ ET AL.	
	Examiner	Art Unit	
	Ja-Na A Hines	1645	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 49-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 49-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group 1, claims 1-13 and 49-56 as restricted in divisional application 09/235,416 is acknowledged.

Amendment Entry

2. Applicants amendment filed November 28, 2000 has been entered. Claims 14-48 and 57-58 have been cancelled. Claims 1-13 and 49-56 are under consideration in this office action.

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The status of nonprovisional parent application (whether abandoned) should also be included. Since the parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Specification

4. The use of the trademark PILEUP™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-13 and 49-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In particular, claim 1 is drawn to an isolated nucleic acid sequence encoding a microtubule motor protein, wherein the protein has the following properties: (i) the protein's activity includes plus end-directed microtubule motor activity; and (ii) the protein has a tail domain that has greater than 60% amino acid sequence identity to a TL-γ tail domain as measured using a sequence comparison algorithm.

The claims and specification fail to provide the identity or structure of this isolated nucleic acid sequence. The specification does not provide evidence of a nucleic acid

sequence, other than the sequence of SEQ ID NO: 2 that can encode a microtubule motor protein. The specification at page 5 lines 7-9 discloses a nucleic acid sequence encoding a plus-end directed microtubule motor protein having a nucleotide sequence of SEQ ID NO: 2; however the specification does not state the identity by nucleic acid sequence or any structural characteristics of any other nucleic acid sequence that has the claimed characteristics. Moreover, there is evidence that other sequences have not yet been identified therefore; applicants' vague description of an isolated nucleic acid sequence has not been adequately described. In view of the lack of evidence, it is apparent that Applicants were not in possession of additional nucleic acid sequences, at the time of filing the instant application.

With the exception of SEQ ID NO: 2, the skilled artisan cannot envision the detailed structure of the isolated nucleic acid sequence, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention. The nucleic acid structure is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. The protein activity characteristics and tail domain requirements distinguish the protein only by what it does, i.e., protein activity, which are purely functional distinctions. Even where there is an actual reduction to practice, which may demonstrate possession of an embodiment of an invention, it does not necessarily describe what the claimed invention is. The instant specification and claims describe an

isolated nucleic acid by its encoded protein function, however this description does not describe the claimed nucleic acid itself.

See also, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), where the court held that a generic statement that defines a genus of nucleic acids by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Thus, in the absence of sequence information of the nucleic acid encoded microtubule motor protein, a nucleic acid described only by its encoded protein activity fails to meet the written description requirements. Therefore only SEQ ID NO:2 and not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph.

With respect to claims drawn to a nucleic acid encoding a microtubule motor protein wherein the protein has the property of having a tail domain that has greater than 60% amino acid sequence identity to a TL-γ tail domain as measured using a sequence comparison algorithm; or a nucleic acid comprising a sequence which has

greater than 60% or 70% sequence identity to nucleotides of SEQ ID NO:2, these claims fails to meet the written description provisions.

Sequences having 60% or 70% sequence identity to SEQ ID NO:2 fail to meet the written description provision of 35 UCS 112, first paragraph. Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, make clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). The specification only discloses SEQ ID NO:2, there is no disclosure of nucleotide sequences with 60% identity of SED ID NO:2. Thus, the structure of these nucleic acid molecules is not defined. Even though the claims recite a sequence identification number, the skilled artisan cannot envision the detailed structure of the encompassed nucleic acid molecules since the specification has not defined what the 30-40% variation can be. There is no requirement of only conservative changes, nor is there a teaching of what regions can or cannot be substituted. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining sequence identity. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

The specification does not provide any representative examples of isolated nucleic acid sequences having 60%-70% identity to SEQ ID NO: 2. There is no teaching or which nucleic acids may or may not be changed without causing detrimental effects towards the production of a microtubule motor protein which retains the recited properties. Applicants have not shown that [redacted] modifying a reference sequence [redacted] will automatically [redacted] encode a microtubule motor protein as claimed. The specification fails to teach the structure or relevant identifying characteristics of a representative number of polynucleotides sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Thus a skilled artisan cannot envision all the contemplated nucleotide sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be achieved until reduction to practice has occurred. Furthermore, *In The Reagents of the University of California v. Eli Lilly*, (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids does not provide an adequate written description of the genus. Applicants are not required to disclose every species encompassed by a genus, thus the description of a genus is achieved by the recitation of a representative number of SEQ ID NO's, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a nucleic acid molecule...'requires a precise definition, such as by structure, formula, chemical name, or physical properties'". However, the specification lacks such examples.

The claims fail to recite the precise definition of the nucleic acid sequence with greater than 60% identity to SEQ ID NO: 2. Currently the generic recitation of 60% identity is insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, the full breadth of the claims fails to meets the written description provision of 35 USC 112, first paragraph.

With respect to claim 7, which is drawn to a nucleic acid sequence wherein the nucleic acid is amplified by primers that selectively hybridize under stringent hybridization conditioned to the primer set of SEQ ID NO:3 and 4, the claims and specification lack sufficient written description of the generically claimed primer. The primer is defined by its activity of function, i.e., the ability to hybridize to SEQ ID NO:3 and 4; with the exception of the primers disclosed in SEQ ID NO:3 and 4. While the description of the ability of the claimed primer to hybridize may describe the primer's function, it does not describe the primer itself. The hybridization distinction is a purely functional distinction. Thus, a description of the primer by what it does, such as hybridizing to SEQ ID NO:3 and 4 is insufficient.

The specification does not provide evidence that any primer, as claimed, functions with the ability to hybridize to SEQ ID NO:3 and 4. There is evidence that other primers have not yet been identified. In view of the lack of evidence, it is apparent that Applicants were not in possession of additional primers, at the time of filing the instant application of such a primer. With the exception of primers identified in SEQ ID

NO: 3 and 4, the skilled artisan cannot envision the detailed structure of the primer, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. The hybridization distinguishes the claimed nucleotide sequences from unclaimed sequences only by what they do, which is a purely functional distinction. Even where there is an actual reduction to practice, which may demonstrate possession of an embodiment of an invention, it does not necessarily describe what the claimed invention is. The instant specification and claims describe a primer is described by its function i.e., hybridization, however this description does not describe the claimed primer itself.

Claim 10 is drawn to an isolated nucleic acid sequence of claim 1 wherein the nucleic acid selectively hybridizes under stringent hybridization ~~conditioned~~ conditions to SEQ ID NO2. The specification and claims lack sufficient written description of hybridization between an unidentified nucleic acid and a target sequence (SEQ ID NO:2) wherein a 40% mismatch is encountered. While the description of the ability of the claimed probe to hybridize to SEQ ID NO:2 may describe the hybridization conditions, it does not describe the either the primer or the target sequence. Again the hybridization distinction is a purely functional distinction. Thus, a description of a generic primer or nucleic acid by what it does, such as hybridizing when an about @ 40% mismatch is encountered is

insufficient. The specification does not appear to teach: hybridization between any primer and SEQ ID NO:2. In view of the lack of evidence, it is apparent that Applicants were not in possession of a method wherein hybridization of up to about a 40% mismatch is encountered. Thus, a skilled artisan cannot envision the detailed structure of the primer and nucleic acid sequence, therefore, conception is not achieved until reduction to practice has occurred.

Thus, in the absence of sequence information of the nucleic acid and primer, which are described only by their ability to hybridize fails to meet the written description requirements. Therefore only the nucleic acid sequence set forth in SEQ ID NO:2 and primers set forth in SEQ ID NO: 3 and 4, and not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

6. Claims 1-13 and 49-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to an isolated nucleic acid sequence encoding a microtubule motor protein, wherein the protein has the following properties: (i) the protein's activity includes plus end-directed microtubule motor activity; and (ii) the protein has a tail domain that has greater than 60% amino acid sequence identity to a TL-γ tail domain as measured using a sequence comparison algorithm or a nucleic acid

sequence comprising a sequence which has greater than 60% sequence identity with SEQ ID NO:2.

The specification at page 5 lines 7-9 discloses a nucleic acid sequence encoding a plus-end directed microtubule motor protein having a nucleotide sequence of SEQ ID NO:2; however the specification does not state the identity by nucleic acid sequence or any structural characteristics of any other nucleic acid sequence that has the claimed characteristics. The specification fails to teach the identity of any other nucleic acid sequences with the claimed abilities. Therefore, the specification fails to enable to an isolated nucleic acid sequence encoding a microtubule motor protein, wherein the protein has the following properties: (i) the protein's activity includes plus end-directed microtubule motor activity; and (ii) the protein has a tail domain that has greater than 60% amino acid sequence identity to a TL-γ tail domain as measured using a sequence comparison algorithm or a nucleic acid sequence comprising a sequence which has greater than 60% sequence identity with SEQ ID NO:2.

There is no teaching of how to determine which of the non-identical nucleotides will contain the 40% mismatch. The specification is not enabled for any variants of a polynucleotide comprising a sequence having 60% identity to SEQ ID NO:2, because the specification fails to teach that such sequences with 60% identity can retain the claimed characteristics; the specification lacks any written description of a structure or relevant identifying characteristics of a representative number of polynucleotides encoding a representative number of proteins sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed; the specification

fails to teach ~~what~~ the critical nucleic acid which can or cannot be modified and still achieve a nucleic acid with the required cross reactivity; or what nucleic acids can be inserted, deleted or substituted within an 60% identical sequence.

The art teaches that replacement of a single nucleic acid residue may lead to both structural and functional changes in the biological activity of a protein. One of skill in the art would be reduced to merely randomly altering nucleic acids which would lead to unpredictable results regarding the cross ~~reactive activity~~ reactivity of the isolated bacterium. The art is replete with examples if one nucleotide is deleted or inserted at a single place within the coding sequence, all codons down stream of that insertion or deletion will be frame shifted; thus it is highly likely that the expression product will have little in common structurally or functionally with the nucleotide sequence of SEQ ID NO:2.

In absence of further guidance from Applicants, the skilled artisan would have to discover what the appropriate additions, deletion and substitutions would be. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use of a sequence having 60% identity to SEQ ID NO:2. The additions/deletions, substitutions or insertions of any nucleic acid in any location within the polynucleotide would not predictably result in the microtubule motor protein containing said polynucleotide sequence. The specification does not provide guidance on how any nucleic acid can be substituted or inserted nor does the specification provide guidance on how any location can be used to produce a stable polynucleotide. No working examples are shown containing the missing

information. Without such information, one of skill in the art could not predict which deletions, substitutions or insertions or any combination would result in the desired polynucleotide. Accordingly, one of skill in the art would be required to perform undue experimentation to use any nucleic acid at any location to produce such a polynucleotide. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

Claim 7 is drawn to a nucleic acid sequence wherein the nucleic acid is amplified by primers that selectively hybridize under stringent hybridization conditions to the primer set of SEQ ID NO:3 and 4. The specification teaches that primers identified as SEQ ID NO:3 and 4 can be used in amplification techniques (page 25 lines 12-15). See also Example I. There is no teaching within the specification of any other primers being used with hybridization techniques. The specification fails to teach examples of any other primers that meet the limitations of the claims. The specification appears to make the conclusion that only the primers of SEQ ID NO:3 and 4 will perform in the hybridization experiments. Therefore, the specification fails to enable other generically claimed primers. The specification does not appear to teach what nucleic acids the generically claimed primers encompass. Furthermore, the specification fails to provide an enabling disclosure for the use of any primer that meets the limitations recited in the claims

Applicants have provided no guidance to enable one of ordinary skill in the art how to make, without undue experimentation, other primers that hybridize. There is no

requirement or limitation for the use of only the primers of SEQ ID NO: 3. Given the lack of guidance contained in the specification and the unpredictability for making primers that hybridizes, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

7. Claims 1-13 and 49-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Acronyms like TL-γ must be spelled out when used for the first time in a chain of claims.

8. ☒ Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a particular algorithm, i.e. PILEUP™ the identification is indefinite. Furthermore, the use of trademarks is improper since products identified by trademarks are within the sole

control of the trademark owner and are subject to change by said owner at their discretion.

Furthermore, claim 6 is indefinite because it recites using the comparison algorithm PILEUP. Applicants have claimed the algorithm that is impermissible and requires deletion because the claim is devoid of any limitation on the manipulation of the phylogenetic parameters. This attempt to incorporate subject matter into the patent by reference is improper because PTO policy does not permit the PTO to exercise any control over algorithm, its alignment methods or the accuracy of the information contained therein. Appropriate correction is required.

9. The term "stringent conditions" in claims 7, 10 and 53-56 is a relative term which renders the claim indefinite. The term "stringent conditions" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus, one cannot determine the metes and bounds of the claim language, therefore the term is indefinite.

10. Claims 8-9 recite the phrase "TL-γ derived from..." however it is unclear how to define "derived from". The specification does not teach how to make derivatives from the recited fungus. The derivative language is vague and indefinite because the characteristics needed to determine whether an unknown could be considered a derivative of the claimed fungus are unknown. The specification neither discloses a

definition for a derived from, nor does it teach a requisite amount of retained qualities needed or characteristics necessary to determine derivatives of the fungus. Therefore the claims are unclear.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
September 3, 2002

LYNETTE R. F. SMITH
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